

EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
S1	589	(548/950).CCLS.	US-PGPUB; USPAT; EPO; DERWENT	OR	OFF	2007/05/31 12:34
S2	341	(548/953).CCLS.	US-PGPUB; USPAT; EPO; DERWENT	OR	OFF	2007/05/31 12:35
S3	2243	(514/422).CCLS.	US-PGPUB; USPAT; EPO; DERWENT	OR	OFF	2007/05/31 12:41
S4	726	(548/527).CCLS.	US-PGPUB; USPAT; EPO; DERWENT	OR	OFF	2007/05/31 12:35
S5	6	((("5495046") or ("6437165") or ("20020042443")).PN.	US-PGPUB; USPAT; EPO; DERWENT	OR	OFF	2007/05/31 12:41

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:SSSPTA1600RXA

PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * Welcome to STN International * * * * *

NEWS	1		Web Page for STN Seminar Schedule - N. America
NEWS	2	JAN 08	CHEMLIST enhanced with New Zealand Inventory of Chemicals
NEWS	3	JAN 16	CA/CAPLUS Company Name Thesaurus enhanced and reloaded
NEWS	4	JAN 16	IPC version 2007.01 thesaurus available on STN
NEWS	5	JAN 16	WPIDS/WPINDEX/WPIX enhanced with IPC 8 reclassification data
NEWS	6	JAN 22	CA/CAPLUS updated with revised CAS roles
NEWS	7	JAN 22	CA/CAPLUS enhanced with patent applications from India
NEWS	8	JAN 29	PHAR reloaded with new search and display fields
NEWS	9	JAN 29	CAS Registry Number crossover limit increased to 300,000 in multiple databases
NEWS	10	FEB 15	PATDPASPC enhanced with Drug Approval numbers
NEWS	11	FEB 15	RUSSIAPAT enhanced with pre-1994 records
NEWS	12	FEB 23	KOREAPAT enhanced with IPC 8 features and functionality
NEWS	13	FEB 26	MEDLINE reloaded with enhancements
NEWS	14	FEB 26	EMBASE enhanced with Clinical Trial Number field
NEWS	15	FEB 26	TOXCENTER enhanced with reloaded MEDLINE
NEWS	16	FEB 26	IFICDB/IFIPAT/IFIUDB reloaded with enhancements
NEWS	17	FEB 26	CAS Registry Number crossover limit increased from 10,000 to 300,000 in multiple databases
NEWS	18	MAR 15	WPIDS/WPIX enhanced with new FRAGHITSTR display format
NEWS	19	MAR 16	CASREACT coverage extended
NEWS	20	MAR 20	MARPAT now updated daily
NEWS	21	MAR 22	LWPI reloaded
NEWS	22	MAR 30	RDISCLOSURE reloaded with enhancements
NEWS	23	APR 02	JICST-EPLUS removed from database clusters and STN
NEWS	24	APR 30	GENBANK reloaded and enhanced with Genome Project ID field
NEWS	25	APR 30	CHEMCATS enhanced with 1.2 million new records
NEWS	26	APR 30	CA/CAPLUS enhanced with 1870-1889 U.S. patent records
NEWS	27	APR 30	INPADOC replaced by INPADOCDB on STN
NEWS	28	MAY 01	New CAS web site launched
NEWS	29	MAY 08	CA/CAPLUS Indian patent publication number format defined
NEWS	30	MAY 14	RDISCLOSURE on STN Easy enhanced with new search and display fields
NEWS	31	MAY 21	BIOSIS reloaded and enhanced with archival data
NEWS	32	MAY 21	TOXCENTER enhanced with BIOSIS reload
NEWS	33	MAY 21	CA/CAPLUS enhanced with additional kind codes for German patents
NEWS	34	MAY 22	CA/CAPLUS enhanced with IPC reclassification in Japanese patents
NEWS EXPRESS			NOVEMBER 10 CURRENT WINDOWS VERSION IS V8.01c, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 25 SEPTEMBER 2006.
NEWS HOURS			STN Operating Hours Plus Help Desk Availability
NEWS LOGIN			Welcome Banner and News Items
NEWS IPC8			For general information regarding STN implementation of IPC 8

Enter NEWS followed by the item number or name to see news on that

specific topic.

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* * * * * STN Columbus * * * * *

FILE 'HOME' ENTERED AT 11:35:40 ON 31 MAY 2007

=> fil reg

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

0.63

0.63

FILE 'REGISTRY' ENTERED AT 11:37:06 ON 31 MAY 2007

USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.

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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 30 MAY 2007 HIGHEST RN 936211-93-7

DICTIONARY FILE UPDATES: 30 MAY 2007 HIGHEST RN 936211-93-7

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH December 2, 2006

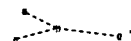
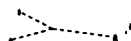
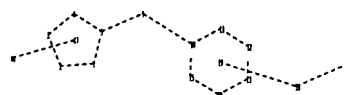
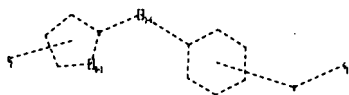
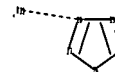
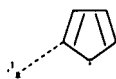
Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

<http://www.cas.org/support/stngen/stndoc/properties.html>

=>

Uploading C:\Program Files\Stnexp\Queries\QUERIES\10500895.str



chain nodes :

9 18 25 31 35 36 37 38 39 40 41 42 46

ring nodes :

1 2 3 4 5 10 11 12 13 14 15 20 21 22 23 24 26 27 28 29 30

chain bonds :

5-9 9-10 18-35 21-25 28-31 36-37 36-38 39-40 39-41 39-42

ring bonds :

1-2 1-5 2-3 3-4 4-5 10-11 10-15 11-12 12-13 13-14 14-15 20-21 20-24

21-22 22-23 23-24 26-27 26-30 27-28 28-29 29-30

exact/norm bonds :

1-2 1-5 2-3 3-4 4-5 5-9 9-10 10-11 10-15 11-12 12-13 13-14 14-15 18-35

20-21 20-24 21-22 21-25 22-23 23-24 26-27 26-30 27-28 28-29 28-31 29-30

36-37 36-38 39-40 39-41 39-42

isolated ring systems :

containing 1 : 10 :

G1: [*1], [*2]

G2: [*3], [*4]

Match level :

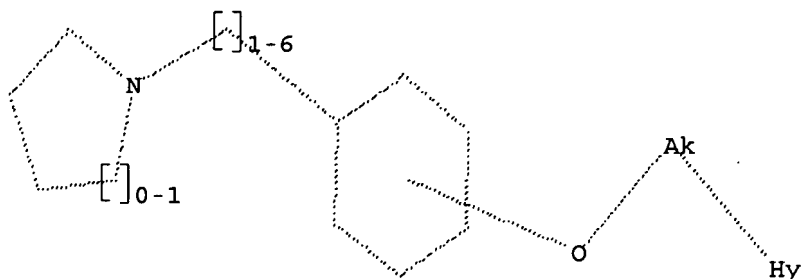
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14:Atom 15:Atom 18:CLASS 19:Atom 20:Atom 21:Atom 22:Atom 23:Atom 24:Atom

25:CLASS 26:Atom 27:Atom 28:Atom 29:Atom 30:Atom 31:CLASS 35:CLASS 36:CLASS

37:CLASS 38:CLASS 39:CLASS 40:CLASS 41:CLASS 42:CLASS 46:CLASS 47:CLASS

```
=> d
L1 HAS NO ANSWERS
L1 STR
```



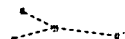
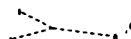
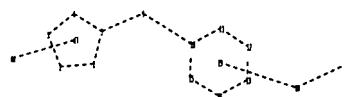
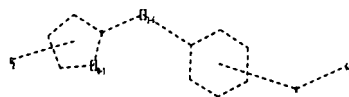
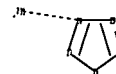
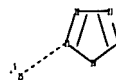
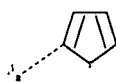
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=> s ll
SAMPLE SEARCH INITIATED 11:43:17 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 443137 TO ITERATE
```

```

FULL FILE PROJECTIONS:  ONLINE  **INCOMPLETE**
                        BATCH    **INCOMPLETE**
PROJECTED ITERATIONS:   8824788 TO 8900692
PROJECTED ANSWERS:      0 TO      0

```

```
=>
Uploading C:\Program Files\Stnexp\Queries\QUERIES\10500895.str
```



chain nodes :

9 18 25 31 35 36 37 38 39 40 41 42 46

ring nodes :

1 2 3 4 5 10 11 12 13 14 15 20 21 22 23 24 26 27 28 29 30

chain bonds :

5-9 9-10 18-35 21-25 28-31 36-37 36-38 39-40 39-41 39-42

ring bonds :

1-2 1-5 2-3 3-4 4-5 10-11 10-15 11-12 12-13 13-14 14-15 20-21 20-24
21-22 22-23 23-24 26-27 26-30 27-28 28-29 29-30

exact/norm bonds :

1-2 1-5 2-3 3-4 4-5 5-9 9-10 10-11 10-15 11-12 12-13 13-14 14-15 18-35
20-21 20-24 21-22 21-25 22-23 23-24 26-27 26-30 27-28 28-29 28-31 29-30
36-37 36-38 39-40 39-41 39-42

isolated ring systems :

containing 1 : 10 :

G1: [*1], [*2]

G2: [*3], [*4]

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 9:CLASS 10:Atom 11:Atom 12:Atom 13:Atom
14:Atom 15:Atom 18:CLASS 19:Atom 20:Atom 21:Atom 22:Atom 23:Atom 24:Atom
25:CLASS 26:Atom 27:Atom 28:Atom 29:Atom 30:Atom 31:CLASS 35:CLASS 36:CLASS
37:CLASS 38:CLASS 39:CLASS 40:CLASS 41:CLASS 42:CLASS 46:CLASS 47:CLASS

L3 STRUCTURE UPLOADED

=> d

L3 HAS NO ANSWERS

L3 STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.

=> s l3

SAMPLE SEARCH INITIATED 11:44:24 FILE 'REGISTRY'

SAMPLE SCREEN SEARCH COMPLETED - 43043 TO ITERATE

4.6% PROCESSED 2000 ITERATIONS

3 ANSWERS

INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**

BATCH **COMPLETE**

PROJECTED ITERATIONS: 848471 TO 873249

PROJECTED ANSWERS: 809 TO 1773

L4 3 SEA SSS SAM L3

=> s l3 full

FULL SEARCH INITIATED 11:44:31 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED - 859967 TO ITERATE

100.0% PROCESSED 859967 ITERATIONS

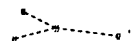
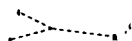
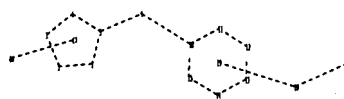
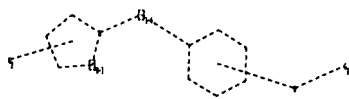
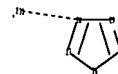
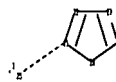
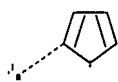
1296 ANSWERS

SEARCH TIME: 00.00.08

L5 1296 SEA SSS FUL L3

=>

Uploading C:\Program Files\Stnexp\Queries\QUERIES\10500895.str



chain nodes :

9 18 25 31 35 36 37 38 39 40 41 42 46

ring nodes :

1 2 3 4 5 10 11 12 13 14 15 20 21 22 23 24 26 27 28 29 30

chain bonds :

5-9 9-10 18-35 21-25 28-31 36-37 36-38 39-40 39-41 39-42

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36-37 36-38 39-40 39-41 39-42

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G2: [*3], [*4]

Match level :

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14:Atom 15:Atom 18:CLASS 19:Atom 20:Atom 21:Atom 22:Atom 23:Atom 24:Atom

25:CLASS 26:Atom 27:Atom 28:Atom 29:Atom 30:Atom 31:CLASS 35:CLASS 36:CLASS

37:CLASS 38:CLASS 39:CLASS 40:CLASS 41:CLASS 42:CLASS 46:CLASS 47:CLASS

L6 STRUCTURE UPLOADED

=> d

L6 HAS NO ANSWERS

L6 STR

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

Structure attributes must be viewed using STN Express query preparation.

=> s l6 subset-l5 full

COMBINATION OF STRUCTURE AND TEXT TERMS NOT VALID

The query entered contains both search terms created by structure-building or screen commands and text search terms. L#s created via the STRUCTURE or SCREEN commands must be searched in the structures files separately from text terms or profiles. The L# answer sets from structure searches can be used in crossover searches and can be combined with text terms.

=> s l6 subset=l5 full

FULL SUBSET SEARCH INITIATED 11:48:20 FILE 'REGISTRY'

FULL SUBSET SCREEN SEARCH COMPLETED - 506 TO ITERATE

100.0% PROCESSED 506 ITERATIONS

27 ANSWERS

SEARCH TIME: 00.00.01

L7 27 SEA SUB=L5 SSS FUL L6

=> s l7 and caplus/lc

54326390 CAPLUS/LC

L8 27 L7 AND CAPLUS/LC

=> fil caplus

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

225.80

226.43

FILE 'CAPLUS' ENTERED AT 11:48:30 ON 31 MAY 2007

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FILE COVERS 1907 - 31 May 2007 VOL 146 ISS 23

FILE LAST UPDATED: 30 May 2007 (20070530/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply. They are available for your review at:

<http://www.cas.org/infopolicy.html>

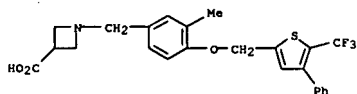
=> s 18

L9 8 L8

=> d ibib abs hitstr 1-8

L9 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2007:262972 CAPLUS
 TITLE: Identification of Leu276 of the S1P1 receptor and Phe263 of the S1P3 receptor in interaction with receptor specific agonists by molecular modeling, site-directed mutagenesis, and affinity studies
 AUTHOR(S): Deng, Qiaolin; Clemas, Joseph A.; Chrebet, Gary; Fischer, Paul; Hale, Jeffrey J.; Li, Zhen; Mills, Sander G.; Bergstrom, James; Mandala, Suzanne; Mosley, Ralph; Parent, Stephen A.
 CORPORATE SOURCE: Department of Molecular Systems, Merck Research Laboratories, Rahway, NJ, USA
 SOURCE: Molecular Pharmacology (2007), 71(3), 724-735
 CODEN: MOPMA3; ISSN: 0026-895X
 PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB Sphingosine-1-phosphate (S1P) receptor agonists are novel immunosuppressive agents. The selectivity of S1P1 against S1P3 is strongly correlated with lymphocyte sequestration and min. acute toxicity and bradycardia. This study describes mol. modeling, site-directed mutagenesis, and affinity studies exploring the mol. basis for selectivity between S1P1 and S1P3 receptors. Computational models of human S1P1 and S1P3 receptors bound with two nonselective agonists or two S1P1-selective agonists were developed based on the x-ray crystal structure of bovine rhodopsin. The models predict that S1P1 Leu276 and S1P3 Phe263 contribute to the S1P1/S1P3 selectivity of the two S1P1-selective agonists. These residues were subjected to site-directed mutagenesis. The wild-type and mutant S1P receptors were expressed in Chinese hamster ovary cells and examined for their abilities to bind to and be activated by agonists in vitro. The results indicate that the mutations have minimal effects on the activities of the two nonselective agonists, although they have dramatic effects on the S1P1-selective agonists. These studies provide a fundamental understanding of how these two receptor-selective agonists bind to the S1P1 and S1P3 receptors, which should aid development of more selective S1P1 receptor agonists with immunosuppressive properties and improved safety profiles.
 IT 570423-80-2
 RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (Identification of Leu276 of S1P1 receptor and Phe263 of S1P3 receptor in interaction with receptor specific agonists by mol. modeling, site-directed mutagenesis, and affinity studies)
 RN 570423-80-2 CAPLUS
 CN 3-Azetidinecarboxylic acid, 1-[[3-methyl-4-[[4-phenyl-5-(trifluoromethyl)-2-thienyl]methoxy]phenyl]methyl]- (CA INDEX NAME)



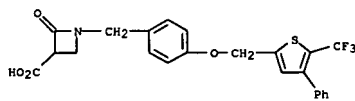
L9 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2006:772794 CAPLUS
 DOCUMENT NUMBER: 145:369215
 TITLE: Species differences in metabolism and pharmacokinetics
 AUTHOR(S): Anari, M. Reza; Creighton, Melissa D.; Ngui, Jason S.; Tschirret-Guth, Richard A.; Teffera, Yohannes; Doas, George A.; Tang, Wei; Yu, Nathan X.; Cicciotto, Suzanne L.; Hobra, Donald F., Jr.; Coleman, John B.; Vincent, Stella H.; Evans, David C.
 CORPORATE SOURCE: Department of Drug Metabolism, Merck Research Laboratories, West Point, PA, USA
 SOURCE: Drug Metabolism and Disposition (2006), 34(8), 1367-1375
 CODEN: DMDSDI; ISSN: 0090-9556
 PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB The pharmacokinetics and metabolism of 1-[[4-[[4-phenyl-5-(trifluoromethyl)-2-thienyl]methoxy]benzyl]azetidine-3-carboxylic acid (MRL-A), a selective agonist for the sphingosine-1-phosphate 1 (S1P1) receptor, were investigated in rats and dogs. In both species, more than 50% of the dose was excreted in bile. Specific to the rat, and observed in bile, were a taurine conjugate of MRL-A and a glucuronide conjugate of an azetidine lactam metabolite. In dogs, a smaller portion of the dose (54% of administered dose) was excreted intact in bile, and the major metabolites detected were an azetidine N-oxide of MRL-A and an acylglucuronide of an N-dealkylation product. This latter metabolite was also observed in rat bile. Stereoselective formation of the N-oxide isomer was observed in dogs, whereas the rat produced comparable amts. of both isomers. The formation of a unique glutathione adduct was observed in rat bile, which was proposed to occur via N-dealkylation, followed by reduction of the putative aldehyde product to form the alc., and dehydration of the alc. to generate a reactive quinone methide intermediate. Incubation of a synthetic standard of this alc. in rat microsomes fortified with reduced glutathione or rat hepatocytes resulted in formation of this unique glutathione adduct.
 IT 910579-67-8 910579-68-9 910579-72-5
 910582-20-6
 RL: BSU (Biological study, unclassified); BIOL (Biological study) (species differences in metabolism and pharmacokinetics of a sphingosine-1-phosphate receptor agonist MRL-A in rats and dogs)
 RN 910579-67-8 CAPLUS
 CN 3-Azetidinecarboxylic acid, 2-oxo-1-[[4-[[4-phenyl-5-(trifluoromethyl)-2-thienyl]methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)

L9 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

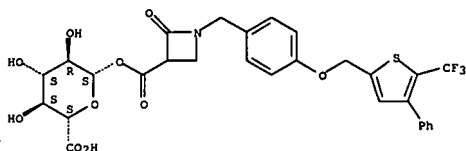
REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RECORD.
 FORMAT

L9 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

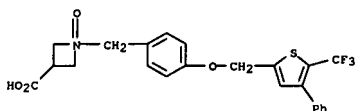


RN 910579-68-9 CAPLUS
 CN β-D-Glucopyranuronic acid, 1-[2-oxo-1-[[4-[[4-phenyl-5-(trifluoromethyl)-2-thienyl]methoxy]phenyl]methyl]-3-azetidinecarboxylate] (9CI) (CA INDEX NAME)

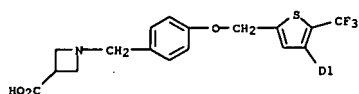
Absolute stereochemistry.



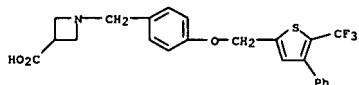
RN 910579-72-5 CAPLUS
 CN 3-Azetidinecarboxylic acid, 1-[[4-[[4-phenyl-5-(trifluoromethyl)-2-thienyl]methoxy]phenyl]methyl]-, 1-oxide (9CI) (CA INDEX NAME)



RN 910582-20-6 CAPLUS
 CN 3-Azetidinecarboxylic acid, 1-[[4-[[4-[[sulfoxy]phenyl]-5-(trifluoromethyl)-2-thienyl]methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)

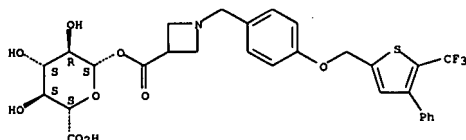
D1-OSO₃H

IT 570423-67-5, MRL-A
 RL: PKT (Pharmacokinetics); BIOL (Biological study)
 (species differences in metabolism and pharmacokinetics of a
 sphingosine-1-phosphate receptor agonist MRL-A in rats and dogs)
 RN 570423-67-5 CAPLUS
 CN 3-Azetidinecarboxylic acid, 1-[[4-[[4-phenyl-5-(trifluoromethyl)-2-
 thienyl]methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)



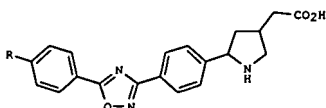
IT 910579-73-6
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (species differences in metabolism and pharmacokinetics of a
 sphingosine-1-phosphate receptor agonist MRL-A in rats and dogs)
 RN 910579-73-6 CAPLUS
 CN β-D-Glucopyranuronic acid, 1-[1-[[4-[[4-phenyl-5-(trifluoromethyl)-2-
 thienyl]methoxy]phenyl]methyl]-3-azetidinecarboxylate] (9CI) (CA INDEX
 NAME)

Absolute stereochemistry.

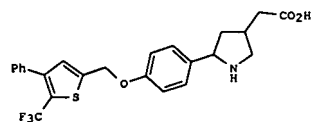


REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR
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ACCESSION NUMBER: 2006:499151 CAPLUS
 DOCUMENT NUMBER: 145:145483
 TITLE: 2-Aryl(pyrrolidin-4-yl)acetic acids are potent
 agonists of sphingosine-1-phosphate (S1P) receptors
 AUTHOR(S): Yan, Lin; Budhu, Richard; Huo, Pei; Lynch,
 Christopher
 L.; Hale, Jeffrey J.; Mills, Sander G.; Hajdu,
 Richard; Keohane, Carol A.; Rosenbach, Mark J.;
 Milligan, James A.; Shei, Gan-Ju; Chretien, Gary;
 Bergstrom, James; Card, Deborah; Mandala, Suzanne M.
 CORPORATE SOURCE: Department of Medicinal Chemistry, Merck Research
 Laboratories, Rahway, NJ, 07065, USA
 SOURCE: Bioorganic & Medicinal Chemistry Letters (2006),
 16(13), 3564-3568
 CODEN: BMCLE8; ISSN: 0960-894X
 PUBLISHER: Elsevier B.V.
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 145:145483
 GI



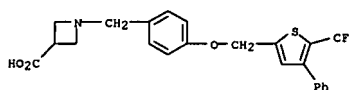
I



II

AB 2-Aryl(pyrrolidin-4-yl)acetic acids I (R = i-Bu, cyclopentyl, cyclohexyl,
 F3C(CH₂)₂, 3,3-difluoro-1-cyclopentyl, 4,4-difluoro-1-cyclohexyl) and II
 were synthesized and their biol. activities as agonists of S1P receptors
 were evaluated. These analogs were able to induce lowering of lymphocyte
 counts in the peripheral blood of mice and were found to have good
 overall
 pharmacokinetic properties in rats.

IT 570423-67-5
 RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); BIOL
 (Biological study)
 (preparation and biol. activity of thiophene- or
 oxadiazole-functionalized
 (aryl)pyrrolidineacetic acids as potent agonists of
 sphingosine-1-phosphate receptors)
 RN 570423-67-5 CAPLUS
 CN 3-Azetidinecarboxylic acid, 1-[[4-[[4-phenyl-5-(trifluoromethyl)-2-
 thienyl]methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR
 THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE
 FORMAT

L9 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:986123 CAPLUS
DOCUMENT NUMBER: 143:431986
TITLE: Discovery of Potent 3,5-Diphenyl-1,2,4-oxadiazole

AUTHOR(S):

Sphingosine-1-phosphate-1 (S1P1) Receptor Agonists with Exceptional Selectivity against S1P2 and S1P3
Li, Zhen; Chen, Weirong; Hale, Jeffrey J.; Lynch, Christopher L.; Mills, Sander G.; Hajdu, Richard; Keohane, Carol Ann; Rosenbach, Mark J.; Milligan, James A.; Shei, Gan-Ju; Chrebet, Gary; Parent,

Stephen

A.; Bergstrom, James; Card, Deborah; Forrest,

Michael;

Quackenbush, Elizabeth J.; Wickham, L. Alexandra; Vargas, Hugo; Evans, Rose M.; Rosen, Hugh; Mandala, Suzanne

CORPORATE SOURCE:

Departments of Medicinal Chemistry and Immunology
Rheumatology Research, Merck Research Laboratories,
Rahway, NJ, 07065, USA

SOURCE:

Journal of Medicinal Chemistry (2005), 48(20),

6169-6173

CODEN: JMCHAR; ISSN: 0022-2623

PUBLISHER:

American Chemical Society

DOCUMENT TYPE:

Journal

LANGUAGE:

English

OTHER SOURCE(S):

CASREACT 143:431986

AB A class of 3,5-diphenyl-1,2,4-oxadiazole based compds. have been identified as potent sphingosine-1-phosphate-1 (S1P1) receptor agonists with minimal affinity for the S1P2 and S1P3 receptor subtypes. Analog 26 (S1P1 IC50 = 0.6 nM) has an excellent pharmacokinetics profile in the rat and dog and is efficacious in a rat skin transplant model, indicating that

S1P3 receptor agonism is not a component of immunosuppressive efficacy.

IT 570423-67-5 570423-80-2

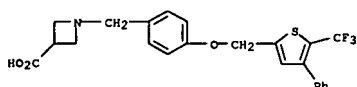
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)

(Discovery of Potent 3,5-Diphenyl-1,2,4-oxadiazole Sphingosine-1-phosphate-1 (S1P1) Receptor Agonists with Exceptional Selectivity)

RN 570423-67-5 CAPLUS

CN 3-Azetidinecarboxylic acid, 1-[[[4-phenyl-5-(trifluoromethyl)-2-thienyl]methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)



RN 570423-80-2 CAPLUS

CN 3-Azetidinecarboxylic acid, 1-[[[3-methyl-4-[[4-phenyl-5-(trifluoromethyl)-2-thienyl]methoxy]phenyl]methyl]- (CA INDEX NAME)

L9 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:1048937 CAPLUS
DOCUMENT NUMBER: 142:147835
TITLE: A Rational Utilization of High-Throughput Screening

AUTHOR(S):

Affords Selective, Orally Bioavailable
1-Benzyl-3-carboxyazetidine Sphingosine-1-phosphate-1

Receptor Agonists
Hale, Jeffrey J.; Lynch, Christopher L.; Neway, William; Mills, Sander G.; Hajdu, Richard; Keohane, Carol Ann; Rosenbach, Mark J.; Milligan, James A.; Shei, Gan-Ju; Parent, Stephen A.; Chrebet, Gary; Bergstrom, James; Card, Deborah; Ferrer, Marc;

Hodder,

Peter; Strulovici, Berta; Rosen, Hugh; Mandala, Suzanne

CORPORATE SOURCE:

Departments of Medicinal Chemistry and Immunology and
Rheumatology Research, Merck Research Laboratories,
Rahway, NJ, 07065, USA

SOURCE:

Journal of Medicinal Chemistry (2004), 47(27),

6662-6665

CODEN: JMCHAR; ISSN: 0022-2623

PUBLISHER:

American Chemical Society

DOCUMENT TYPE:

Journal

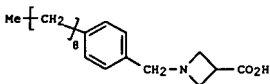
LANGUAGE:

English

OTHER SOURCE(S):

CASREACT 142:147835

GI



I

AB Moderately potent, selective S1P1 receptor agonists identified from high-throughput screening have been adapted into lipophilic tails for a class of orally bioavailable amino acid-based S1P1 agonists represented by

1. Many of the new compds. are potent S1P1 agonists that select against the S1P2, S1P3, and S1P4 (although not S1P5) receptor subtypes. Two of the analogs are highly orally bioavailable and possess excellent pharmacokinetic profiles in the rat, dog, and rhesus monkey.

IT 570423-67-5P 570423-76-6P 570423-80-2P

RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN

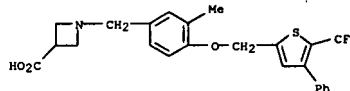
(Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP

(Preparation); USES (Uses)
(1-benzyl-3-carboxyazetidine derivs. as EDG-1 receptor agonists and immunosuppressants: high-throughput screening for oral bioavailability and preparation)

RN 570423-67-5 CAPLUS

CN 3-Azetidinecarboxylic acid, 1-[[[4-phenyl-5-(trifluoromethyl)-2-thienyl]methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)

L9 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



REFERENCE COUNT:

28

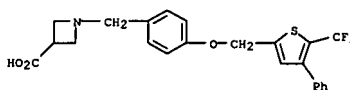
THERE ARE 28 CITED REFERENCES AVAILABLE FOR

THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

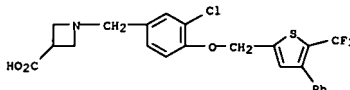
L9 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 570423-76-6 CAPLUS

CN 3-Azetidinecarboxylic acid,

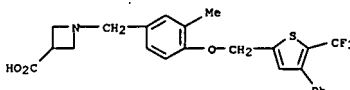
1-[[[3-chloro-4-[[4-phenyl-5-(trifluoromethyl)-2-thienyl]methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)



RN 570423-80-2 CAPLUS

CN 3-Azetidinecarboxylic acid,

1-[[[3-methyl-4-[[4-phenyl-5-(trifluoromethyl)-2-thienyl]methoxy]phenyl]methyl]- (CA INDEX NAME)



IT 570423-45-9P 570423-78-8P 828269-16-5P

828269-17-6P 828269-18-7P 828269-19-8P

828269-20-1P 828269-21-2P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU

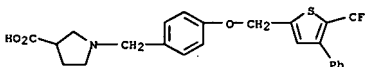
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

(Uses)
(1-benzyl-3-carboxyazetidine derivs. as EDG-1 receptor agonists and

immunosuppressants: high-throughput screening for oral bioavailability and preparation)

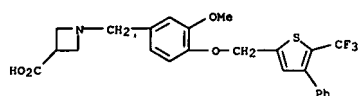
RN 570423-45-9 CAPLUS

CN 3-Pyrrolidinecarboxylic acid, 1-[[[4-phenyl-5-(trifluoromethyl)-2-thienyl]methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)

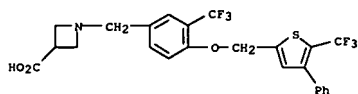


L9 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2007 ACS ON STN (Continued)

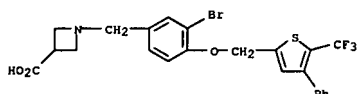
RN 570423-78-8 CAPLUS
CN 3-Azetidinecarboxylic acid, 1-[[3-methoxy-4-[[4-phenyl-5-(trifluoromethyl)-2-thienyl]methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)



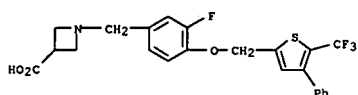
RN 828269-16-5 CAPLUS
CN 3-Azetidinecarboxylic acid, 1-[[4-[[4-phenyl-5-(trifluoromethyl)-2-thienyl]methoxy]-3-(trifluoromethyl)phenyl]methyl]- (9CI) (CA INDEX NAME)



RN 828269-17-6 CAPLUS
CN 3-Azetidinecarboxylic acid, 1-[[3-bromo-4-[[4-phenyl-5-(trifluoromethyl)-2-thienyl]methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)



RN 828269-18-7 CAPLUS
CN 3-Azetidinecarboxylic acid, 1-[[3-fluoro-4-[[4-phenyl-5-(trifluoromethyl)-2-thienyl]methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)

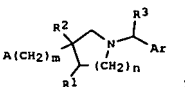


RN 828269-19-8 CAPLUS
CN 3-Azetidinecarboxylic acid, 1-[[3-ethyl-4-[[4-phenyl-5-(trifluoromethyl)-2-thienyl]methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)

L9 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2007 ACS ON STN
ACCESSION NUMBER: 2003:591193 CAPLUS
DOCUMENT NUMBER: 139:149520
TITLE: Preparation of aralkylpyrrolidines and -azetidines as Edg receptor agonists
INVENTOR(S): Bugianesi, Robert L.; Doherty, George A.; Gentry, Amy;
Sander: Hale, Jeffrey J.; Lynch, Christopher L.; Mills, G.; Neway, William E., III
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 112 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

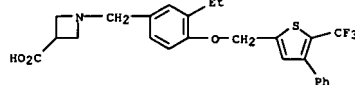
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003062252	A1	20030731	WO 2003-US1196	20030115
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2472715	A1	20030731	CA 2003-2472715	20030115
EP 1470137	A1	20041027	EP 2003-705779	20030115
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2005515259	T	20050526	JP 2003-562129	20030115
US 2005033055	A1	20050210	US 2004-500895	20040707
PRIORITY APPLN. INFO.:			US 2002-350000P	P 20020118
			WO 2003-US1196	W 20030115

OTHER SOURCE(S): MARPAT 139:149520
G1

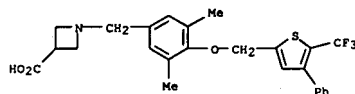


AB Title compds. I [Ar = (un)substituted Ph, naphthyl; A = CO2H, P(O)(OH)2, P(O)OH, SO3H, 1H-tetrazol-5-yl; R1, R2 = H, halogen, OH, CO2H, (un)substituted alkyl; R3 = H, (un)substituted alkyl; m, n = 0, 1] were prepared for use as Edg receptor agonists, useful for treating immune mediated diseases and conditions, such as bone marrow, organ and tissue

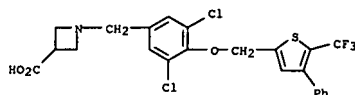
L9 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2007 ACS ON STN (Continued)



RN 828269-20-1 CAPLUS
CN 3-Azetidinecarboxylic acid, 1-[[3,5-dimethyl-4-[[4-phenyl-5-(trifluoromethyl)-2-thienyl]methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)

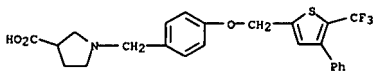


RN 828269-21-2 CAPLUS
CN 3-Azetidinecarboxylic acid, 1-[[3,5-dichloro-4-[[4-phenyl-5-(trifluoromethyl)-2-thienyl]methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)

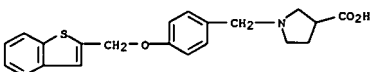


REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

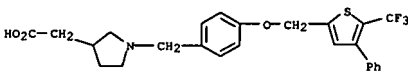
L9 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2007 ACS ON STN (Continued)
transplant rejection (no data). Thus, 3-pyrrolidinol was converted to di-Et 3-hydroxypyrrolidin-3-ylphosphonate and treated with 4-nonylbenzaldehyde, followed by ester hydrolysis to give 1-(4-nonylbenzyl)-3-hydroxypyrrolidine-3-phosphonic acid.
IT 570423-45-9P 570423-58-4P 570423-65-3P 570423-67-5P 570423-73-3P 570423-74-4P 570423-75-5P 570423-76-6P 570423-77-7P 570423-78-8P 570423-79-9P 570423-80-2P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of aralkylpyrrolidines and -azetidines as Edg receptor agonists)
RN 570423-45-9 CAPLUS
CN 3-Pyrrolidinecarboxylic acid, 1-[[4-[[4-phenyl-5-(trifluoromethyl)-2-thienyl]methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)



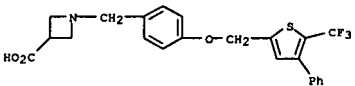
RN 570423-58-4 CAPLUS
CN 3-Pyrrolidinecarboxylic acid, 1-[[4-(benzo[b]thien-2-yl)methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)



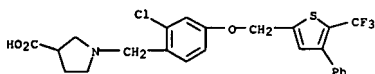
RN 570423-65-3 CAPLUS
CN 3-Pyrrolidinecarboxylic acid, 1-[[4-[[4-phenyl-5-(trifluoromethyl)-2-thienyl]methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)



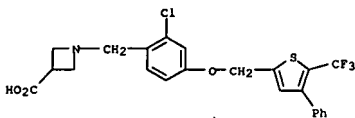
RN 570423-67-5 CAPLUS
CN 3-Azetidinecarboxylic acid, 1-[[4-[[4-phenyl-5-(trifluoromethyl)-2-thienyl]methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)



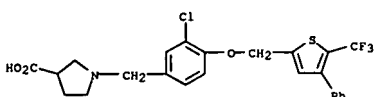
L9 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2007 ACS ON STN (Continued)
RN 570423-73-3 CAPLUS
CN 3-Pyrrolidinecarboxylic acid, 1-[[2-chloro-4-[[4-phenyl-5-(trifluoromethyl)-2-thienyl]methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)



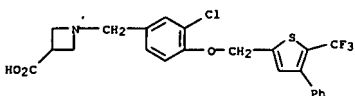
RN 570423-74-4 CAPLUS
CN 3-Azetidinecarboxylic acid, 1-[[2-chloro-4-[[4-phenyl-5-(trifluoromethyl)-2-thienyl]methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)



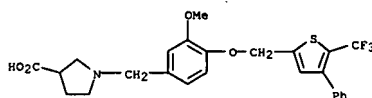
RN 570423-75-5 CAPLUS
CN 3-Pyrrolidinecarboxylic acid, 1-[[3-chloro-4-[[4-phenyl-5-(trifluoromethyl)-2-thienyl]methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)



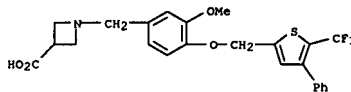
RN 570423-76-6 CAPLUS
CN 3-Azetidinecarboxylic acid, 1-[[3-chloro-4-[[4-phenyl-5-(trifluoromethyl)-2-thienyl]methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)



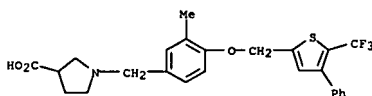
L9 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2007 ACS ON STN (Continued)
RN 570423-77-7 CAPLUS
CN 3-Pyrrolidinecarboxylic acid, 1-[[3-methoxy-4-[[4-phenyl-5-(trifluoromethyl)-2-thienyl]methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)



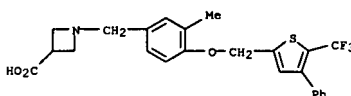
RN 570423-78-8 CAPLUS
CN 3-Azetidinecarboxylic acid, 1-[[3-methoxy-4-[[4-phenyl-5-(trifluoromethyl)-2-thienyl]methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)



RN 570423-79-9 CAPLUS
CN 3-Pyrrolidinecarboxylic acid, 1-[[3-methyl-4-[[4-phenyl-5-(trifluoromethyl)-2-thienyl]methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)



RN 570423-80-2 CAPLUS
CN 3-Azetidinecarboxylic acid, 1-[[3-methyl-4-[[4-phenyl-5-(trifluoromethyl)-2-thienyl]methoxy]phenyl]methyl]- (CA INDEX NAME)



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS

L9 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2007 ACS ON STN (Continued)
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L9 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2007 ACS ON STN
ACCESSION NUMBER: 2003:590932 CAPLUS
DOCUMENT NUMBER: 139:149413
TITLE: Selective S1P1/Edg1 receptor agonists
Doherty, George A.; Forrest, Michael J.; Hajdu,
Richard; Hale, Jeffrey J.; Li, Zhen; Mandala, Suzanne
M.; Mills, Sander G.; Rosen, Hugh; Scolnick, Edward
M.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 202 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003061567	A2	20030731	WO 2003-US1120	20030114
WO 2003061567	A3	20031224		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GR, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MM, ME, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
US 2004058894	A1	20040325	US 2003-339380	20030109
CA 2472680	A1	20030731	CA 2003-2472680	20030114
EP 1469863	A2	20041027	EP 2003-731917	20030114
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK			
US 2005070506	A1	20050331	US 2004-501176	20040712
PRIORITY APPLN. INFO.:			US 2002-349991P	P 20020118
			US 2002-362566P	P 20020307
			US 2002-382933P	P 20020523
			WO 2003-US1120	W 20030114

AB The present invention encompasses a method of treating an immunoregulatory abnormality in a mammalian patient in need of such treatment comprising administering to said patient a compound which is an agonist of the S1P1/Edg1 receptor in an amount effective for treating said immunoregulatory abnormality, wherein said compound possesses a selectivity for the S1P1/Edg1 receptor over the S1PR3/Edg3 receptor, said compound administered in an amount effective for treating said immunoregulatory abnormality. Thus, 4-HOC6H4CHO was treated with Me(CH2)7I to give 4-Me(CH2)7OC6H4CHO which was treated with H2N(CH2)3P(O)(OH)2 to give 4-Me(CH2)7OC6H4CH2NH(CH2)3P(O)(OH)2 which had an EC50 for S1P1 agonism of 1.5 nM and for S1P3 agonism of 6.0 nM.
IT 570423-45-9P 570423-58-4P 570423-65-3P 570423-67-5P 570423-73-3P 570423-74-4P

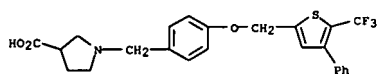
L9 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2007 ACS ON STN (Continued)

570423-75-5P 570423-76-6P 570423-77-7P
570423-78-8P 570423-79-9P 570423-80-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
(Uses)

(prepn. of amino functionalized organo phosphonates or organo
carboxylates as S1P1/Edg1 receptor agonists)

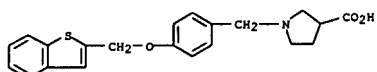
RN 570423-45-9 CAPLUS

CN 3-Pyrrolidinecarboxylic acid, 1-[[[4-(phenyl-5-(trifluoromethyl)-2-thienyl)methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)



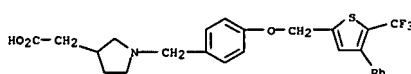
RN 570423-58-4 CAPLUS

CN 3-Pyrrolidinecarboxylic acid, 1-[[[4-(benzo[b]thien-2-ylmethoxy)phenyl]methyl]- (9CI) (CA INDEX NAME)



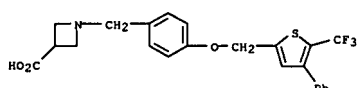
RN 570423-65-3 CAPLUS

CN 3-Pyrrolidinecarboxylic acid, 1-[[[4-(phenyl-5-(trifluoromethyl)-2-thienyl)methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)



RN 570423-67-5 CAPLUS

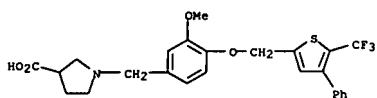
CN 3-Azetidinecarboxylic acid, 1-[[[4-(phenyl-5-(trifluoromethyl)-2-thienyl)methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)



RN 570423-73-3 CAPLUS

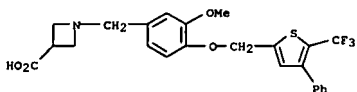
CN 3-Pyrrolidinecarboxylic acid, 1-[[[2-chloro-4-[[4-phenyl-5-(trifluoromethyl)-2-thienyl)methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)

L9 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2007 ACS ON STN (Continued)



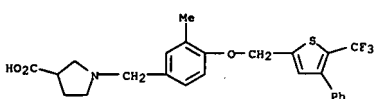
RN 570423-78-8 CAPLUS

CN 3-Azetidinecarboxylic acid, 1-[[[3-methoxy-4-[[4-phenyl-5-(trifluoromethyl)-2-thienyl)methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)



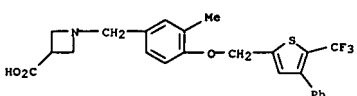
RN 570423-79-9 CAPLUS

CN 3-Pyrrolidinecarboxylic acid, 1-[[[3-methyl-4-[[4-phenyl-5-(trifluoromethyl)-2-thienyl)methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)

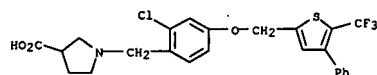


RN 570423-80-2 CAPLUS

CN 3-Azetidinecarboxylic acid, 1-[[[3-methyl-4-[[4-phenyl-5-(trifluoromethyl)-2-thienyl)methoxy]phenyl]methyl]- (CA INDEX NAME)

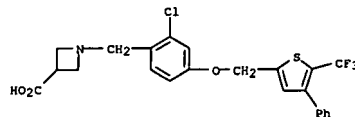


L9 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2007 ACS ON STN (Continued)



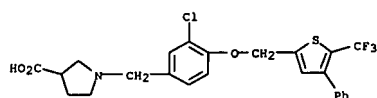
RN 570423-74-4 CAPLUS

CN 3-Azetidinecarboxylic acid, 1-[[[2-chloro-4-[[4-phenyl-5-(trifluoromethyl)-2-thienyl)methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)



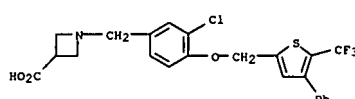
RN 570423-75-5 CAPLUS

CN 3-Pyrrolidinecarboxylic acid, 1-[[[3-chloro-4-[[4-phenyl-5-(trifluoromethyl)-2-thienyl)methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)



RN 570423-76-6 CAPLUS

CN 3-Azetidinecarboxylic acid, 1-[[[3-chloro-4-[[4-phenyl-5-(trifluoromethyl)-2-thienyl)methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)



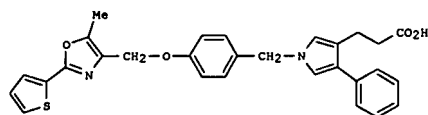
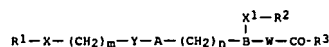
RN 570423-77-7 CAPLUS

CN 3-Pyrrolidinecarboxylic acid, 1-[[[3-methoxy-4-[[4-phenyl-5-(trifluoromethyl)-2-thienyl)methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)

L9 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2007 ACS ON STN

ACCESSION NUMBER: 2001:396864 CAPLUS
DOCUMENT NUMBER: 135:19632
TITLE: Preparation of pyrazolyl- and pyrrolylalkanoic acid derivatives with hypoglycemic and hypolipidemic activity
INVENTOR(S): Momose, Yu; Maekawa, Tsuyoshi; Odaka, Hiroyuki; Kimura, Hiroyuki
PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., Japan
SOURCE: PCT Int. Appl., 375 pp.
CODEN: FIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

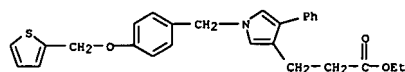
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001038325	A1	20010531	WO 2000-37877	20001109
W:	AE, AG, AL, AM, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CU, CZ, DE, DK, EE, EG, ES, FI, FR, GB, GR, HU, ID, IL, IN, IS, JP, KR, KZ, LC, LK, LR, LT, LV, MA, MD, MG, MK, MN, MX, MY, NZ, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, US, UZ, VN, YU, ZA			
RW:	GH, GN, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
CA 2390923	A1	20010531	CA 2000-2390923	20001109
JP 200126350	A	20010821	JP 2000-347462	20001109
JP 3723071	B2	20051207		
BR 2000015466	A	20020806	BR 2000-15466	20001109
EP 1228067	A1	20020807	EP 2000-974857	20001109
EP 1228067	B1	20040714		
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
HU 200203165	A2	20030128	HU 2002-3165	20001109
JP 2003137865	A	20030514	JP 2002-315096	20001109
NZ 519238	A	20031128	NZ 2000-519238	20001109
AT 271049	T	20040715	AT 2000-974857	20001109
EP 1457490	A1	20040915	EP 2004-76508	20001109
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
PT 1228067	T	20041130	PT 2000-974857	20001109
ES 2225252	T3	20050316	ES 2000-974857	20001109
AU 780948	B2	20050428	AU 2001-13031	20001109
RU 2252939	C2	20050527	RU 2002-115263	20001109
NO 200202108	A	20020708	NO 2002-2108	20020502
US 7179823	B1	20070220	US 2002-129702	20020509
IN 2002KN0645	A	20050311	IN 2002-KN645	20020513
ZA 2002003824	A	20031015	ZA 2002-3824	20020514
HK 1045991	A1	20041210	HK 2002-106297	20020827
PRIORITY APPL. INFO.:			JP 1999-320317	A 19991110
			JP 1999-352237	A 19991210
			JP 1999-352236	A 19991210
			EP 2000-974857	A3 20001109
			JP 2000-347462	A3 20001109
			WO 2000-37877	W 20001109



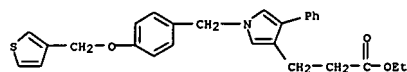
AB Title compds. (I) [wherein R1 = (un)substituted hydrocarbon or heterocycle; X = bond, O, S, CO, CS, CR4(OR5), or NR6; R4 and R6 = independently H or (un)substituted hydrocarbon; R5 = H or hydroxyl protective group; m = 0-3; Y = O, S, SO, SO2, NR7, CONR7, or NR7CO; R7 = H or (un)substituted hydrocarbon; A = (un)substituted aromatic ring; n = 1-8; B = (un)substituted N-containing 5-membered heterocycle; X1 = bond, O, S, SO, SO2, or NR16; R16 = H or (un)substituted hydrocarbon; R2 = H or (un)substituted hydrocarbon or heterocycle; W = bond or hydrocarbon; R3 = OR8 or NR9R10; R8 = H or (un)substituted hydrocarbon; R9 and R10 = independently H or (un)substituted hydrocarbon or heterocycle; or R9 and R10 together with the N to which they are attached may form a ring] were prepared as retinoid-related receptor function regulating agents or insulin resistance improving agents. For example, Et 3-[1-(4-hydroxybenzyl)-4-phenyl-3-pyrrolyl]propionate and 4-chloromethyl-5-methyl-2-(2-thienyl)oxazole were coupled in the presence of K2CO3 in DMF and treated with HCl to give II (77%). At a concentration of 0.001%, II reduced hypoglycemic and hypolipidemic action by 48% and 70%, resp., lowered total cholesterol by 16%, and increased the plasma anti-arterioclerosis index by 12% compared to non-treatment groups of mice. In addition, II showed potent PPARγ-RXRα heterodimer ligand activity with EC50 of 1.5 nM. I are useful for the prevention or treatment of diabetes mellitus, hyperlipidemia, impaired glucose tolerance, inflammatory diseases, and arteriosclerosis.

IT 342025-29-OP 342025-31-4P
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses) (preparation of pyrrolyl- and pyrazolylalkanoic acid derivs. as retinoid X receptor and PPAR receptor modulators)

RN 342025-29-0 CAPLUS
 CN 1H-Pyrrole-3-propanoic acid, 4-phenyl-1-[[4-(2-

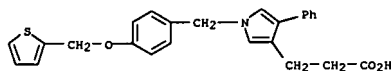


RN 342025-31-4 CAPLUS
 CN 1H-Pyrrole-3-propanoic acid, 4-phenyl-1-[[4-(3-thienylmethoxy)phenyl]methyl]-, ethyl ester (9CI) (CA INDEX NAME)

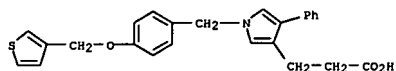


IT 342025-30-3P 342025-32-5P
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (preparation of pyrrolyl- and pyrazolylalkanoic acid derivs. as retinoid X receptor and PPAR receptor modulators)

RN 342025-30-3 CAPLUS
 CN 1H-Pyrrole-3-propanoic acid, 4-phenyl-1-[[4-(2-thienylmethoxy)phenyl]methyl]- (9CI) (CA INDEX NAME)



RN 342025-32-5 CAPLUS
 CN 1H-Pyrrole-3-propanoic acid, 4-phenyl-1-[[4-(3-thienylmethoxy)phenyl]methyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

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COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

42.63

269.06

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE

TOTAL

ENTRY

SESSION

CA SUBSCRIBER PRICE

-6.24

-6.24

STN INTERNATIONAL LOGOFF AT 11:48:53 ON 31 MAY 2007